

## Estimation of Breast Doses and Breast Cancer Risk Associated with Repeated Fluoroscopic Chest Examinations of Women with Tuberculosis<sup>1</sup>

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A methodology is presented to estimate cumulative breast dose and breast cancer risk for women exposed to repeated fluoroscopic chest examinations during air collapse therapy for pulmonary tuberculosis. Medical record abstraction, physician interview, patient contact, machine exposure measurements, and absorbed dose computations were combined to estimate average breast doses for 1047 Massachusetts women who were treated between 1930 and 1954. The methodology presented considers breast size and composition, patient orientation, X-ray field size and location, beam quality, type of examination, machine exposure rate, and exposure time during fluoroscopic examinations. The best estimate for the risk of radiation-induced cancer for the women living longer than 10 years after initial fluoroscopic exposure is 6.2 excess breast cancers per million woman-year-rad with 90% confidence limits of 2.8 and 10.7 cancers/10<sup>6</sup> WY-rad. When breast cancer risk is considered as a function of absorbed dose in the breast, instead of as a function of the number of fluoroscopic examinations, a linear dose-response relationship over the range of estimated doses is consistent with the data. However, because of the uncertainty due to small-sample variability and because of the wide range of assumptions regarding certain fluoroscope conditions, other dose-response relationships are compatible with the data.

### INTRODUCTION

To estimate the possible radiation hazard associated with periodic X-ray mammography examinations, risk estimates of radiation-induced breast cancer

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(1) have been applied that derive from studies of atomic bomb survivors in Japan (2-4), acute postpartum mastitis patients treated with therapeutic X rays in New York (5, 6), and tuberculosis patients subjected to multiple fluoroscopes during air collapse therapy of the lung in Nova Scotia (7). None of these series, however, represents a population that has been exposed under conditions similar to those under which women undergoing periodic mammography, are exposed, i.e., low-energy (25-50 kVp) and low-dose diagnostic X-ray examinations repeatedly performed over a number of years. The atomic bomb irradiation was a single whole-body exposure to high-energy  $\gamma$  rays and neutrons. The mastitis patients were treated for a breast disease by therapeutic X rays (175-270 kVp), and the radiation was delivered in one to several high-dose fractions over a period of about a week. The women with tuberculosis, on the other hand, received repeated low-energy (70-85 kVp) and relatively-low-dose fluoroscopic exposures to diagnostic X rays that continued for an average of 3-5 yr. The estimation of the radiation dose received by the Nova Scotia women was, however, so unreliable that the National Academy of Sciences chose the value of the postpartum mastitis study, six cases of breast cancer/106 woman-year-rad<sup>5</sup>, as their best estimate of the absolute risk for radiation-induced breast cancer (1).

To augment existing data on risk estimates for the induction of breast cancer by ionizing radiation (1-7), a followup study was conducted of pulmonary tuberculosis patients in two Massachusetts hospitals who received repeated fluoroscopic examinations of the chest during air collapse treatments of the lung (pneumothorax and pneumoperitoneum) (8). To obtain information on the cumulative breast doses received by these patients, an extensive methodology, described in this report, was developed. These dose estimates were derived by abstracting information from medical records, interviewing physicians, contacting patients, measuring X-ray exposures from representative fluoroscopes, and applying an absorbed dose calculation scheme that employs a Monte Carlo radiation transport technique. Average absorbed breast doses were estimated for each patient fluoroscopically examined. On the basis of the observed frequency of breast cancers in the exposed population, estimates of breast cancer risk were made, and the resulting dose-response relationship was examined.

## SUBJECTS AND METHODS

### *Study Population*

Female patients who were discharged alive from two Massachusetts hospitals between 1930 and 1954 were studied (8). The numbers of pneumothorax or pneumoperitoneum treatments were determined from the hospital records, and 1047 women were designated as exposed individuals. The comparison group

<sup>5</sup> Absolute risk estimates as presented in the BEIR report (1) derive from the following calculations:  $(O - E) / [(WY)(D)]$  where  $O$  = observed cases,  $E$  = expected cases,  $WY$  = woman-years at risk for breast cancer development, and  $D$  = average breast dose in rad. The absolute excess risk estimate is specific for the years of followup included in the calculation. The postpartum mastitis estimate excludes the first 10 yr of followup, and is applicable for years 10 to 29 after initial exposure.

TABLE I  
Sanatorium X-Ray Experience

	<i>Exposed group</i>	<i>Comparison group</i>
Number of women	1047	717
Fluoroscopy exams (av)	102	—
Years fluoroscoped (av)	3.3	—
Exams/year	31	—
Chest X rays (av)	49	30
X Rays/year as an:		
In patient	5.1	5.8
Out patient	2.1	1.8

consisted of 717 sanatorium patients who did not receive air collapse therapy and the associated repeated fluoroscope exposures.

For patients undergoing pneurnotherapy, air was injected into the pleural or peritoneal cavity in order to collapse the lung. For a period of several years, additional air was required every 1–3 weeks, and a fluoroscopic examination was conducted each time to determine the quantity of air needed to maintain the lung collapse. Table I shows the X-ray experience of the study population. The exposed women averaged 102 fluoroscopic examinations each, and air collapse treatment continued for an average of 3.3 yr. The exposed women averaged 49 radiographic chest X rays versus 30 for the comparison group.

#### *Patient Questionnaire*

A mail questionnaire was sent to the 1146 women found alive as of July 1975. Of the 675 exposed women who were sent the questionnaire, 543 responded. These 675 women were asked whether they remembered the physician's fluoroscopic procedure. Specifically, the patient was queried about whether she faced the physician or had her back to him during the fluoroscope, whether her orientation varied, and whether she was rotated. Table II presents the responses to

TABLE II  
Patient Questionnaire

Questionnaires sent to exposed subjects	675
Questionnaire responses	543
Questionnaire usable responses to position question	341 (100%)
Omitted 96	
Forgot 59	
Not asked 47 (pilot questionnaire)	
Position when fluoroscopically examined	
Faced the M.D.	213 (63%)
Faced X-ray tube	56 (16%)
Varied	72 (21%)
Rotated during fluoroscopy: 41 (12%)	

TABLE III

Fluoroscopy Procedures as Determined by Physician Interview

Number of physicians	15
Years as tuberculosis physician	
Average	13 yr
Range	2-25 yr
Patients given air without fluoroscopy	<1%
Patients fluoroscoped after refill	1%
Patients fluoroscoped facing X-ray tube	29%
Patients rotated during fluoroscopy	20%
Fluoroscopy performed with shutters open	69%
Opposite lung also scanned	81%
Time for fluoroscopy examination	
Average	15 sec
Range	3-60 sec

the patient questionnaire: 63% faced the physician during a fluoroscope, 16% faced the X-ray tube, and 21% had variable orientations (12% reported being rotated).

#### Physician Interview

To obtain detailed information on the actual conditions during the fluoroscopic examinations, 15 former tuberculosis physicians who had performed air collapse therapies and one former radiological technician were contacted. Tables III and IV present the results of these interviews. It was determined that (1) 29% of the physicians fluoroscopically examined the patient with her chest (breasts) to the X-ray tube; (2) 69% conducted fluoroscopic examinations with the X-ray beam shutters wide open and 81% always scanned the opposite lung to determine whether the tuberculosis had spread; (3) the average time of a fluoroscopic examination was 15 sec (with responses ranging from 3 to 60 sec); (4) 70 to 80

TABLE IV

X-Ray Field Conditions Selected to Be Consistent with Radiological Practice, 1930-1954

Projection	X-Ray field center			X-Ray field (width × height at image Receptor) (cm)
	Distance from phantom vertex (cm)	Distance from nearest anatomical landmark	Distance from phantom midline (cm)	
Pneumothorax, shutters open	42.4	7.6 cm above xiphoid process	0	40.6 × 27.9
Pneumothorax, shuttered beam	42.4	7.6 cm above xiphoid process	10	20.3 × 27.9
Pneumoperitoneum	52	2 cm below xiphoid process	0	40.6 × 24.1
Chest X ray	42.4	7.6 cm above xiphoid process	0	35.6 × 43.2

kVp and 5 mA were the usual 'machine parameters; and (5) 1 mm of aluminum filtration was added in 1948.

Information with regard to three different fluoroscopic field sizes was also obtained. In order to specify the X-ray fields on the phantom used in the absorbed dose calculations, the physicians were asked to sketch the body areas that would be included in the X-ray field during specific fluoroscopic examinations. The X-ray fields selected to be compatible with these sketches are summarized in Table IV.

#### *Fluoroscope Exposure Measurements*

Laboratory measurements were made on three representative fluoroscopy units: a Victor (G. E. ) Vertical Fluoroscope, Model B751 (1922), a Fisher Vertical Fluoroscope, Type X (1925), and a Picker Vertical Fluoroscope, Style T-10 (1935). One of the fluoroscopes had never been operated until a few years ago. Exposure rates at the fluoroscope panel and first half-value layers were determined for various peak kilovoltages and added aluminum filtrations. The experimental data are tabulated in Table V and presented in Fig. 1. The kilovoltages listed were measured using a sphere gap having 3.5-in. spheres, and the milliamperage readings were checked for accuracy. Under similar operating conditions and at given kilovoltages and filtrations, all three systems provided essentially identical exposure rates.

From personal experience [E. D.T.], it is known that all fluoroscopes of this period used a 12- to 13-in. (30.5- to 33.0-cm) distance from the tube focal spot to the panel. Shorter distances could not be used since the high-voltage terminals were exposed and shorter distances would have led to arcing to the supporting structure. The 5-30 tube, later called the RB tube, was used in a lightproof lead glass shield. When the so-called autoprotective tube, the XP, became available, it was used because it provided better X-ray shielding. A mounted cone was provided that placed the focal spot at the same distance from the panel as was the case with the RB tube.

The RB tube, when operated on self-rectified equipment, could be operated continuously at 85 kVp and 5 mA for 6 min in any 36-rein interval. Operation at lower kilovoltages would permit slightly longer operating times; however, long exposures were impossible as they would permanently damage the fluoroscope tube.

Table V and Fig. 1 can be used to determine patient exposure if operating conditions are known. For example, if a fluoroscope were operated with no added filtration at 75 kVp and 5 mA for an average exposure time of 15 sec, the patient entrance skin exposure measured free-in-air would be (10.2 R/mA-min) (5 mA) (0.25 rein) = 12.75 R.

A fluoroscope used to monitor the lung collapse of the Massachusetts women in this study was also located in a private physician's office. Exposure rates determined for various machine settings were within 6% agreement with the controlled fluoroscopic measurements made in the laboratory.

The exposure measurements were summarized into average conditions for each of two time periods to be consistent with fluoroscopic practice before and after

TABLE V

Exposure Rate at Panel, First HVL, and Kilovolt Peaks for Selected Autotransformer Settings and Added Aluminum Filtration<sup>a</sup>

Autotrans- former setting	kVp	Added filter (mm Al)	First HVL (mm Al)	Exposure rate	
				R/min	R/mA-min
4	58	0	0.7	30.2	6.05
		0.5	1.05	18.2	3.65
		1.0	1.3	12.7	2.55
		2.0	1.65	7.5	1.5
		3.0	2.0	4.8	0.96
8	63	0	0.75	36.2	7.2
		0.5	1.15	22.2	4.45
		1.0	1.4	15.7	3.1
		2.0	1.75	9.6	1.9
		3.0	2.15	6.6	1.3
12	68	0	0.8	42.0	8.4
		0.5	1.15	26.7	5.35
		1.0	1.5	18.9	3.8
		2.0	1.8	11.7	2.35
		3.0	2.35	8.1	1.6
18	75	0	0.9	51.2	10.2
		0.5	1.25	32.9	6.6
		1.0	1.55	24.1	4.8
		2.0	2.0	15.8	3.15
		3.0	2.45	11.2	2.25
26	85	0	1.0	63.2	12.6
		0.5	1.4	40.7	8.15
		1.0	1.7	31.6	6.3
		2.0	2.2	21.1	4.2
		3.0	2.75	15.2	3.05

<sup>a</sup> General Electric Vertical Fluoroscope 5 mA, (8 × 10)-in. field at panel.

1948 (Table VI). The exposure rate at the panel for all patients fluoroscopically examined before 1948 was assigned the value of 51.2 R/rein for an unfiltered X-ray beam. A panel exposure rate of 24.1 R/rein was assigned for a 1-mm added aluminum-filtered beam for all patients receiving fluoroscopes during and after 1948.

#### *Absorbed Dose in the Breast*

Estimates of absorbed dose in the breast were derived from a Monte Carlo radiation transport technique, a method that simulates and records the energy deposition of X-ray photons as they undergo physical interactions in an anthropomorphic phantom (9). When the technique is applied to simulate the

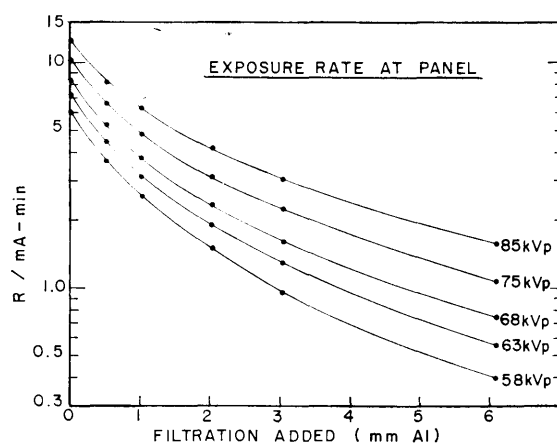


FIG. 1. Exposure rate ( $R/\text{mA}\cdot\text{min}$ ) at fluoroscope panel for various kilovoltage and filtration conditions.

interaction of diagnostic X rays in human tissue, the physical processes treated are the photoelectric effect and Compton scattering. The initial energies of the X-ray photons used during air collapse fluoroscopes were less than 100 keV.

The anthropomorphic phantom represents a reference human and is heterogeneous. It consists of skeletal, lung, and tissue regions with corresponding compositions and densities. The important human organs are mathematically formulated within the phantom and are the interaction sites of interest. Energy depositions are accumulated at these sites. The average absorbed dose in the organ of interest is obtained directly by dividing the accumulated energy by the mass of the organ.

For the present study, the phantom was modified to include the female breasts as described below. X-ray spectral distributions representing the beam qualities of interest were also employed as well as exposure geometries used during the fluoroscope examinations. The details of the Monte Carlo technique and the phantom, as applied generally with diagnostic X-ray photon energies, have been previously described (9).

Two categories of patient breast size were modeled in the anthropomorphic phantom, an adolescent and an adult. The shape of the breast was simulated by

TABLE VI

Fluoroscopy Conditions Selected to Be Consistent with Pneumotherapy Practices

Beam quality	75 kVp
X-Ray tube current	5 mA
Tube-to-panel distance	33 cm
Exposure rate at panel	
Before 1948, unfiltered beam (HVL = 0.9 mm Al)	51.2 R/min
After 1948, 1 mm aluminum added filtration (HVL = 1.55 mm Al)	24.1 R/min

one-half an ellipsoid of revolution attached to the chest wall of the existing phantom with the following dimensions: adolescent breast, 3-cm distance from chest wall to nipple and 3.75-cm diameter at the chest wall, 22.3 g each; adult breast, 6-cm distance from chest wall to nipple and 7.5-cm diameter at the chest wall, 179 g each. The remainder of the phantom serves as a backscattering medium in the AP orientation and as a shielding medium (20 cm thick) in the PA orientation. The composition of all breasts was that of average glandular tissue: 10.5% hydrogen, 23.0% carbon, 2.3% nitrogen, 63.2% oxygen, and various smaller percentages of other trace elements (9). As a result of physician interviews and the relatively young age of most patients, it was decided that these assumptions were consistent with the observation that patients with sufficiently serious tuberculosis to require pneumothorax therapy were generally thin and deficient in both subcutaneous and mammary fat. If the composition of breast were assumed to include a proportion of mammary fat (e. g., 50% adipose and 50% glandular), the resulting decrease in absorbed dose would be less than 15% for all conditions.

To simulate the beam qualities selected as representative of patient treatment (Table VI), X-ray spectra were measured on laboratory X-ray sources using germanium detectors (10). The kilovolt peak and HVL values were matched with those in Table VI, resulting in the X-ray spectra tabulated in Table VII.

The absorbed dose (rad) in the breast per 1 R of entrance skin exposure (free-in-air) was calculated for each breast for 16 selected exposure situations (Table VIII).<sup>6</sup> The absorbed dose in the breast is defined as the total energy deposited in the breast volume divided by the total breast mass.

These 16 selected exposure situations (Table VIII) take into account the following factors: (1) 2 beam qualities (Table VI); (2) 2 patient orientations (AP, radiation incident on the anterior skin surface, or PA, radiation incident on the posterior skin surface); (3) 2 breast sizes (adult or adolescent), and (4) 4 X-ray field sizes and locations (Table IV).

For example, an adult woman facing the X-ray tube (AP) before 1948 (unfiltered, 0.9 mm Al HVL beam) would receive a right-breast dose of 0.412 rad and a left-breast dose of 0.005 rad for each 1 R of entrance skin exposure if the physician shuttered the X-ray beam during a right-lung pneumothorax fluoroscope.

<sup>6</sup> Recent experimental measurements (13) of absorbed dose in the breast utilizing an Alderson-Rando phantom, Mix-D breast simulations (as described above) and multiple locations of lithium fluoride dosimeters (TLD-100) are in good agreement with the Monte Carlo computed breast dose values. The X-ray beam qualities, geometries, and exposure conditions were maintained constant for both the experiment and computations. For the AP view, in which the breast is directly exposed, the absorbed dose is about 0.5 rad/R and agreement was within 2%. As the AP view is the overwhelming contributor of breast dose, this comparison is the most meaningful. For the PA view, in which the X rays are attenuated by 20 cm of intervening inhomogeneous tissues, the absorbed dose is about 0.02 rad/R and agreement was poorer (20 to 50%). In the light of experimental and computational uncertainties involved with the reduced dose from a PA view and also the differences in the composition of the experimental and mathematical phantoms, the discrepancy is not surprising. Regardless, the PA view contributes only a small fraction of the total breast dose among those patients fluoroscopically examined, and the effect of such a difference is minimal.



TABLE VII  
X-Ray Spectra Used in Absorbed Dose Calculation

Photon energy (keV)	Relative number of photons <sup>a</sup>	
	75 kVp, 0.9 mm Al HVL	75 kVp, 1.55 mm Al HVL
8	0.0002	0.0026
10	0.0650	0.0099
12	0.1498	0.0294
14	0.3093	0.0812
16	0.5647	0.2053
18	0.7705	0.3949
20	0.8989	0.5788
22	0.9810	0.7509
24	1.0000	0.8750
26	0.9907	0.9558
28	0.9492	1.0000
30	0.8986	0.9989
32	0.8435	0.9896
34	0.7893	0.9599
36	0.7292	0.9227
38	0.6704	0.8701
40	0.6226	0.8163
42	0.5704	0.7641
44	0.5165	0.7038
46	0.4707	0.6441
48	0.4303	0.5919
50	0.3922	0.5396
52	0.3512	0.4897
54	0.3169	0.4439
56	0.2822	0.3959
58	0.2741	0.3581
60	0.2423	0.3199
62	0.1891	0.2557
64	0.1610	0.2065
66	0.1351	0.1702
68	0.1144	0.1250
70	0.0764	0.0701
72	0.0468	0.0274
74	0.0100	0.0075

<sup>a</sup> Normalized to 1 photon at peak energy.

### Fluoroscope Doses

To determine cumulative patient breast doses from fluoroscopic examinations, the information obtained from individual medical records, physician interview, patient contact, exposure measurements, and absorbed dose calculations was utilized. From the medical records the age at examination, year of examination, type of examination, and lung(s) collapsed (right, left, or bilateral) were determined. Females under 17 yr of age were assigned absorbed doses consistent with the adolescent breast size, and women aged 17 yr and older were assigned doses

TABLE VIII

Breast Dose (Expressed as rad per 1 R of Entrance Skin Exposure Free-in-Air)  
for 16 Selected Radiologic Conditions

<i>Breast size</i>	<i>Beam quality (Table VI) (mm Al HVL)</i>	<i>Field size</i>	<i>Patient orientation with respect to X-ray tube</i>	<i>Average breast dose (rad/R)</i>	
				<i>Right breast</i>	<i>Left breast</i>
Adult	0.9	Shuttered pneumothorax	AP <sup>a</sup>	0.412 <sup>b,c</sup>	0.005
Adult	1.55	Shuttered pneumothorax	AP	0.456 <sup>b</sup>	0.007
Adult	0.9	Unshuttered pneumothorax	AP	0.482	0.482
Adult	1.55	Unshuttered pneumothorax	AP	0.559	0.559
Adult	1.55	Pneumoperitoneum	AP	0.012	0.012
Adolescent	0.9	Shuttered pneumothorax	AP	0.698 <sup>b</sup>	0.004
Adolescent	1.55	Shuttered pneumothorax	AP	0.794 <sup>b</sup>	0.005
Adolescent	0.9	Unshuttered pneumothorax	AP	0.769	0.769
Adolescent	1.55	Unshuttered pneumothorax	AP	0.810	0.810
Adult	0.9	Shuttered pneumothorax	PA	0.015 <sup>b</sup>	0.002
Adult	1.55	Shuttered pneumothorax	PA	0.022 <sup>b</sup>	0.002
Adult	0.9	Unshuttered pneumothorax	PA	0.017	0.017
Adult	1.55	Unshuttered pneumothorax	PA	0.022	0.022
Adult	0.9	Chest X-ray	PA	0.043	0.043
Adult	1.55	Chest X-ray	PA	0.048 <sup>d</sup>	0.048
Adult	1.55	Pneumoperitoneum	PA	0.005	0.005

<sup>a</sup> Patient faces X-ray tube during AP orientation.

<sup>b</sup> In presence of right lung pneumothorax.

<sup>c</sup> The coefficients of variation for calculated rad/R values of 0.412 or greater are 1.5 to 4.0%.

<sup>d</sup> The coefficients of variation for calculated rad/R values of 0.048 or less are 9.0 to 30.0%.

consistent with the adult breast size. Examinations before 1948 were assigned exposure rates and absorbed doses for an unfiltered beam; fluoroscopes during and after 1948 were assigned corresponding values for a filtered beam (Table VI). The field size was determined by the type of examination (Table IV).

Except for the few questionnaire respondents who recalled their orientation with respect to the fluoroscope X-ray source, individual orientations could not be determined. Considering the physician and patient questionnaire responses (Tables II, III) it was decided to assume that 25% of all examinations were

performed in the AP position (with the patient facing the X-ray tube) and 75% in the PA position. During a unilateral lung collapse, both breasts were assumed to be in the X-ray beam 81% of the time (unshuttered) (Table 111), whereas 19% of the time only one breast was assumed exposed (shuttered). In the latter case, average breast doses were computed by adding the dose received by the exposed breast and the scatter dose received by the opposite breast and dividing by 2. For the few cases in which both lungs were collapsed (bilateral), both breasts were exposed 100% of the time during fluoroscope. The average time for a fluoroscope examination was assumed to be 15 sec.

If an adult woman had received 10 pneumothorax examinations before 1948, her estimated cumulative breast dose would be computed as: [(10 exams) (51.2 R/rein) (0.25 rein/exam)] {0.81 [0.25(0.482 rad/R) + 0.75(0.017 rad/R)] + 0.19[0.25(0.412 + 0.005 rad/R)/2 + 0.75(0.015 + 0.002 rad/R)/2]} = 15.2 rad.

It should be noted that "average" breast doses were computed for each individual on the basis of the best estimates of average orientation and average fluoroscopy practices obtained through patient and physician enquiry. As individual breast doses could be estimated for only a small number of patients, it was decided to compute average doses for all individuals. Initially an attempt was made to utilize individually identifiable information but it was unsuccessful. Many of the 269 patients with presumed known orientation were treated by physicians who had died, and therefore fluoroscope information was unattainable. It was also common for patients institutionalized for many years to have been treated by several physicians, not all of whom were interviewed. Coupled with the obvious difficulty in relying on individual patient and physician memories of 20 to 45 yr ago, it seemed prudent to use the "average" values of all patient and physician responses for estimating breast doses for all patients.

## RESULTS

### *Breast Cancer and Number of Fluoroscopic Examinations*

Fifty-six histologically confirmed breast cancer cases among all study subjects were ascertained. Figure 2 shows the standardized incidence rates of breast cancer, adjusted for age at exposure and duration of followup, as a function of

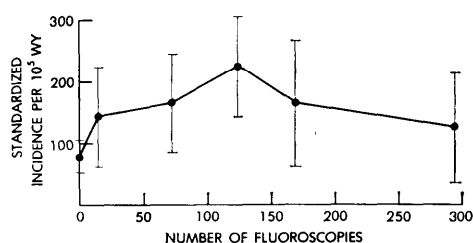


FIG. 2. Standardized incidence of breast cancer per 100,000 woman-years (WY) at risk adjusting for age at exposure and duration of followup, by number of fluoroscopic examination; 80% confidence limits presented.

TABLE IX  
Observed and Expected Breast Cancer Cases and Women-Years at  
Risk by Average Breast Dose

	Average breast dose (rad)						Total <sup>a</sup>
	0	1-99	100-199	200-299	300-399	400+	
Mean dose (rad)	0	32	151	242	344	574	
Number of women	717	469	251	177	65	62	1047
Breast cancer cases							
Observed	15	10	12	12	3	4	41
Expected <sup>b</sup>	14.1	9.6	5.7	4.8	1.5	1.1	23.3
Woman-years at risk (WY)	19,025	10,990	7097	5584	2020	1735	28,011
Standardized incidence per 10 <sup>5</sup> WY <sup>c</sup>	79	109	165	225	144	354	159

<sup>a</sup> Includes unknown dose category, and excludes 0-rad comparison patients.

<sup>b</sup> Expected values computed using Connecticut age-calendar year specific breast cancer incidence rates.

<sup>c</sup> Comparing the exposed patients with the 0-rad comparison patients, adjusting for age at exposure and duration of followup.

number of fluoroscopic examinations (8). The comparison patients were used as the standard. An increased risk is suggested for those receiving less than 50 fluoroscopes, but the increase is not statistically significant ( $P = 0.5$ , 1 tail). A decrease in risk among those receiving 150 or more fluoroscopes is also suggested. Distribution of risk by number of fluoroscopes, however, fails to take into account the previously mentioned factors that contribute to the magnitude of absorbed dose in the breast.

#### Breast Cancer and Cumulative Absorbed Dose

Observed and expected breast cancer cases and woman-years at risk as a function of cumulative breast dose (rad) are presented in Table IX, and standard-

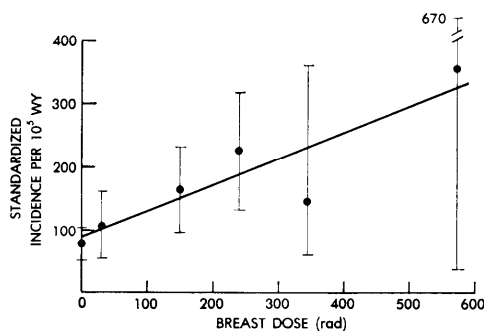


FIG. 3. Standardized incidence of breast cancer per 100,000 woman-years (WY) at risk adjusting for age at exposure and duration of followup, by estimated cumulative breast dose. Best-fitting least-squares line and 80% confidence limits presented.

ized breast cancer incidence rates in Fig. 3. No decrease in risk at high doses (574 rad) is apparent, and a dose-response relationship that increases linearly or otherwise continuously with increasing dose is not inconsistent with the data [ $X_1^2$  (trend) = 7.6,  $P = 0.003$ ]. The confidence limits are wide, however, and other patterns are possible. (Figure 3 differs somewhat from a previously published dose-response curve (8) in that incidence rates of the "nonexposed" tuberculosis patients are used as the standard instead of Connecticut Tumor Registry rates.)

#### *Risk Estimate*

A single fluoroscopic examination was estimated to result in an average absorbed dose to the breast of 1.5 rad, and each individual received an estimated cumulative breast dose of approximately 150 rad on the average. The Massachusetts women in this study, living 10 yr or more since first fluoroscopic exposure, are estimated to have a breast cancer risk of 6.2 radiation-induced breast cancer cases per million woman-year-rad, with 90% Poisson confidence limits of 2.8 and 10.7 cancers/ $10^6$  WY-rad (Table X).

It is important to examine each assumption made in deriving the above risk

TABLE X  
Average Breast Doses and Resulting Risk Estimates as a Function of the  
Assumptions Regarding Fluoroscopic Practice

<i>Assumption</i>	<i>Estimated average breast dose per subject (rad)</i>	<i>Risk estimate<sup>b</sup> CA/106 WY-rad</i>
Best estimate <sup>a</sup>	149	6.2
Breast size		
Adolescent (3 cm)	208	4.5
Adult (6 cm)	136	6.8
Aluminum beam filtration		
Inherent, only	166	5.6
1 mm added	90	10.3
X-Ray field size		
Unshuttered	167	5.5
Shuttered	75	12.4
Time for exam (sec)		
20	199	4.7
10	100	9.3
5	50	18.5
Patient orientation (% facing X-ray tube)		
100	543	1.7
30	175	5.3
20	123	7.5
0	18	51.5

<sup>a</sup> Assumption: Adolescent breast size for those under 17 yr of age at first exposure; 1 mm Al added in 1948; 81 % of the exams performed unshuttered; 15-sec exam time; 2570 of the exams performed with patients facing the X-ray tube.

<sup>b</sup> Computed as  $(O - E) / \{ (WY) (\text{dose}) \}$ , i.e.,  $(38 - 20.85) / \{ (18, 511) (\text{estimated dose}) \}$ . (The first 10 yr of observation have been excluded.)

estimate in order to determine the range of possible risk estimates that could result if different fluoroscope conditions were assumed. Table X lists the average breast doses and resulting risk estimates as a function of the various assumptions regarding fluoroscopic practice. If the total population of exposed women had breast sizes equivalent to the "adolescent size," the average breast dose would be higher, 208 rad, and the risk estimate lower, 4.5/10<sup>6</sup> WY-rad. Different assumptions regarding X-ray field size, examination time, or patient orientation would also have an appreciable effect on the breast dose estimate and risk estimate. If a 10- or 20-sec average exposure time were assumed instead of 15 sec, the absolute risk estimates would have been 9.3 and 4.7 cases/10<sup>6</sup> WY-rad, respectively. In addition to exposure time, another critical determinant of breast dose would be whether the patient faced the X-ray tube and received direct breast irradiation or whether she faced the physician. If the patients were assumed to have been fluoroscope 20 or 30% of the time facing the X-ray tube, instead of 25%, the absolute excess risk estimates would be 7.5 and 5.3 cancers/10<sup>6</sup> WY-rad, respectively. Considering all the factors contributing to radiation dose, the risk estimate for the women in this study is probably between 3 and 11 excess breast cancers per 10<sup>6</sup> WY-rad.

The contribution to breast dose of multiple radiographic chest X-ray examinations was not included in the risk calculations because the resulting dose was so small. Entrance exposure measured free-in-air was 185 mR for the following typical exposure conditions: 73 kVp, 100 mA,  $\frac{1}{5}$ -sec exposure, 72-in. (183-cm) focal spot-to-film distance, no added filtration, HVL = 0.9 mm Al. For one PA chest X-ray the resulting breast dose was calculated to be 0.008 rad. For the woman exposed to repeated fluoroscopic examinations, the average number of chest X-ray examinations (49) would contribute only 0.4 rad to their estimated cumulative breast dose of 150 rad.

#### DISCUSSION

Previous estimates of cumulative breast dose from pneumothorax fluoroscope have been crude and have resulted in questionable breast cancer risk estimates (1). <sup>7</sup>The methodology presented in this report has attempted to improve the estimation of fluoroscopic breast doses by combining information from physician interview, patient questionnaire response, and machine exposure measurements with an absorbed dose computation. Allowing for the assumptions concerning actual fluoroscopic conditions to vary, the best estimate of excess breast cancer absolute risk (6.2 cases/10<sup>6</sup> WY-rad) is likely to be accurate within sampling variation (3 to 11 cases/10<sup>6</sup> WY-rad).

The breast cancer risk estimates presented, however, were made assuming no uncertainty in the estimated cumulative breast dose. This is a tenuous assumption because of the difficulty in retrospectively estimating fluoroscope procedures and doses, and the risk estimates obtained should be interpreted with some caution.

<sup>7</sup>Breast doses from pneumothorax fluoroscopes have also been recently estimated for two fluoroscopes used in the 1940s in Canada. A chipboard phantom and TLD dosimeters were employed and depth-dose curves were determined. The number of tuberculosis patients studied was small, however, and no excess breast cancers were observed and no risk estimates were determined (14).

Similarly, the estimated average breast dose per fluoroscopic examination was calculated by adding the doses received by both breasts and dividing by 2. This concept of average dose to the total organ system has been used in two previous human studies (5,11). Nevertheless, the concept may be questioned, particularly when the breasts are unevenly or partially irradiated. In addition, if the distribution of radiosensitive tissue in the breast is not uniform, computing the radiation dose using total breast volume may not be the most appropriate approach. No other method of estimating breast dose, however, was deemed practical.

Table XI compares the findings of the current Massachusetts fluoroscope study with the three previously mentioned studies. The risk estimate for the Massachusetts tuberculosis patients is comparable with the two studies of Western women but about three times larger than the estimate from the Japanese population exposed to atomic radiation. One explanation is a variation in genetic susceptibility. Alternative explanations for this difference might be that the Japanese risk estimate is diluted because of the inclusion of the low-risk post-exposure years 5 to 9 in the risk computation. Because the Japanese study has a maximum period of observation of 25 yr, it is also possible that the risk estimate will increase with the passage of time, as suggested in the current study (8). These two factors alone could possibly explain the difference in risk estimates. If the risk estimate for the Massachusetts women in our study were calculated considering only years 5 to 24 of followup, the absolute risk estimate would have been 3.1 cases/ $10^6$  WY-rad, in close agreement with the Japanese estimate of 2.5 cases/ $10^6$  WY-rad.

The Western studies also involved populations of women whose mean ages at first exposure were 7–9 yr younger than the Japanese women. If age at exposure is inversely related to breast cancer risk (8), the older atomic bomb victims may in fact be at lower risk. The Japanese women also received “whole-body” radiation exposure, and if the resulting ovarian irradiation had a protective effect on breast cancer development, the risk estimate obtained would be lower than the estimate from those studies involving partial-body irradiation. In studies of women undergoing radiation cast ration (12), significant decreases in death due to breast cancer have been observed that could be attributable to ovarian irradiation.<sup>8</sup>

Although the absolute risk estimate derived from our study of Massachusetts fluoroscope patients can be supported with some confidence, a number of dose-response relationships could be consistent with the data. The variation of breast cancer incidence rate by the number of fluoroscopic examinations suggests a falloff of risk at the higher cumulative doses. In the Nova Scotia fluoroscope study, no falloff was seen and breast cancer incidence increased with increasing numbers of fluoroscopic examinations up through the maximum average number of 450 (1). No falloff was observed in the present study either, when the breast cancer incidence rate was expressed as a function of cumulative patient breast dose (rad) rather than the number of fluoroscopic examinations. Conversion to cumulative breast dose included the effect of important variables such as orienta-

<sup>8</sup>In animal studies, however, mammary neoplasia can be increased when only the ovaries of mice are irradiated (16); whereas, no effect on mammary neoplastic development attributable to ovarian irradiation is apparent following “whole-body” radiation exposure of rats (16).

TABLE XI  
Risk Estimates for Breast Cancer Induction by Radiation and Comparisons with Other Studies

	<i>Number irradiated</i>	<i>Woman-years used for risk calculation</i>	<i>Type of radiation</i>	<i>Duration of exposure</i>	<i>Age at exposure range (mean)</i>	<i>Breast dose in rad range (mean)</i>	<i>Time after irrad. on which risk estimates are based (years)</i>	<i>Relative risk (O/E)</i>	<i>Cancers induced per 10<sup>6</sup> WY-rad (90% CL)</i>
Atomic bomb survivors <sup>a</sup> (1, 3, 4)	11,968	235,345	Gamma ray and neutron	Less than 10 sec	10+ (34)	10-450 (61)	5-24	82/48.5 =1.7	2.5 (1.3, 3.6)
Nova Scotia fluoroscopy series (1, 6)	243	3,708	Diagnostic X ray, 70-85 kVp	Weeks to years	0-60+ (26)	50-7,000 (1215)	10-30	10.5	8.4 <sup>b</sup>
Mastitis patients (1, 5, 12)	606	9,301	Therapeutic X ray, 175-250 kVp	Minutes to weeks	15-44 (27)	40-1,200 (247)	10-34	36/16.2 =2.2	8.3 (3.1, 16.0)
Current Massachusetts fluoroscopy study	1,047	18,511	Diagnostic X ray, 70-85 kVp	Days to years	5-55 (25)	1-1,027 (150)	10-44	38/20.9 =1.8	6.2 (2.8, 10.7)

<sup>a</sup> Women over 10 yr of age at irradiation who received greater than 9 rad of breast kerma dose.

<sup>b</sup> Confidence limits (CL) cannot be calculated.



tion, beam filtration, and type of examination. The sample size and the associated confidence limits on the breast cancer incidence rates are such that dose-response functions other than linear could be compatible with the data. Although no clear-cut dose-response function is evident, the data are consistent with linearity and it appears prudent to assume a linear relationship for the purpose of radiation protection and public health considerations (1).

When comparing the exposed patients with the comparison patients and adjusting for age at exposure and duration of followup (Table IX), it is interesting that a risk associated with breast doses under 100 rad is suggested: The standardized incidence rate of breast cancer among those receiving an average of 32 rad is  $109/10^5$  versus  $79/10^5$  WY for the comparison patients. This increase, however, is not statistically significant ( $P = 0.47$ , 1 tail). When Connecticut incidence rates are used to compute expected breast cancer cases (Table IX), no excess breast cancer is apparent among those receiving less than 100 rad (10 cancers observed and 9.6 expected). These data, however, should not be interpreted to mean that there is *no* risk for breast cancer induction at these dose levels. The sample size of 469 women and the average breast dose of 32 rad may have been too small to detect a statistically significant increased risk. On the basis of a risk estimate of 6.2 cancers/ $10^6$  WY-rad, an excess of 1.4 radiogenic breast cancers would have been expected for these 469 women. There is no statistically significant difference between the observed 10 cases and the predicted  $(9.6 + 1.4) = 11$  cancers based on the radiation risk estimate.

Data from the previous fluoroscope study of Nova Scotia tuberculosis patients were consistent with a linear dose-response relationship between breast cancer incidence and high total breast doses attained from many individual low-dose fractions (1). Because all the Nova Scotia women faced the X-ray tube during fluoroscope examination, the cumulative breast doses were great, averaging 1215 rad. The range of cumulative breast doses for the Massachusetts patients in our study (150-rad average), however, is approximately one magnitude lower than that for the Nova Scotia series. The results of the two studies, with regard to the shape of the dose-response curve and the computed breast cancer risk estimates, are compatible. This suggests that for low-dose fractionated exposures, the breast cancer risk per rad is similar over a wide range of total cumulative doses.

The fluoroscope studies also present overall radiation risk estimates that are similar to those derived from studies involving single or few radiation exposures (2-5). The repeated fluoroscopic exposures, however, were delivered over a period of years, allowing cellular repair and repopulation to occur. Since these multiple low-dose exposures might be expected to produce fewer deleterious effects than a single exposure of the same total dose (1), the fact that they do not suggests that the radiation damage is cumulative. When assessing the possible radiation risk associated with repeated low-dose mammography exposures, it appears prudent to assume that the risk is present at the low dose levels involved and that the total risk will be proportional to the total radiation dose received during the lifetimes of the women exposed,

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